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EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,148	SEIDMAN, MICHAEL D.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-21 is/are rejected.

7)☒ Claim(s) 1-21 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3 August 2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are presented for examination.

Applicant's Information Disclosure Statement filed August 3, 2004 has been received and entered into the application. As reflected by the attached, completed copy (3 pages total), the Examiner has considered the cited references.

Claim Objections

Claims 3 and 10 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 3, for example, is drawn to the composition of claim 1, wherein the lipoic acid comprises alpha-lipoic acid. However, the Examiner has noted that claim 1 expressly recites the use of alpha-lipoic acid and, thus, dependent claim 3 fails to further limit the subject matter of claim 1. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 1 is objected to for not setting forth the claim limitations in a clear manner. Applicant is requested to amend the following limitation of the claim for clarity: "...with the proviso that the composition lipoic acid and the acetyl-L-carnitine are not administered together." e.g., by deleting "composition".

Claims 1, 3, 7-8, 11, 13, 16-17 and 20 are objected to for failing to consistently refer to "+/- alpha-lipoic acid" as such. See, for example, claim 7 at line 3, where it is referred to as "lipoic acid". All instances of "lipoic acid" should be changed accordingly to ---+/- alpha-lipoic acid---.

Claim 20 is objected to for the following minor informality: the phrase "...amounts at least two components..." should be amended to read "...amounts **of** at least two components..." for clarity.

Claim 21 is objected to for claiming "a method of claim 19", wherein claim 19 is drawn to a composition. Applicant is requested to amend the claim by correcting the dependency of the claim. **For the purposes of examination, claim 21 will be considered dependent on claim 20**.

Claims 2-19 are objected to for claiming "the composition of claim 1", wherein claim 1 is drawn to "a nutritional supplement". All dependent claims should consistently refer back to the same invention, i.e., in this case "a nutritional supplement", for consistency. Applicant is requested to amend the claims appropriately.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

(i) the specification does not contain corresponding disclosure of the dosage ranges of claims 7-8, 11 and 16-17. The following dose ranges do not have support in the specification: 50-7000 mg acetyl-L-carnitine (see claims 7 and 8); 40-1000 mg resveratrol (see claim 7 and 16); 50-7000 mg acetyl-L-carnitine (see claim 8); 600-3000 mg +/- alpha lipoic acid (see claims 11, 16 and 17); 250-2000 mg acetyl-L-carnitine (see claims 11, 16 and 17); 100-750 mg N-acetyl cysteine (see claims 11 and 16); 250-2000 mg acetyl-L-carnitine (see claims 16 and 17); and

100-7500 mg N-acetyl cysteine (see claim 17). Appropriate correction to the disclosure is required.

The disclosure is objected to because of the following informalities:

(i) the acronyms "COX" and "SDH" at page 3, line 3 of the disclosure and the acronym "ADAS" at page 22, line 13 of the disclosure should be defined at their first occurrence in the specification; and

(ii) the phrase "mtDNA del" at page 18, line 4 of the disclosure should be defined at its first occurrence in the specification.

Appropriate correction is required.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chopra (U.S. Patent No. 6,300,377 B1; 2001) in view of Stedman's Medical Dictionary (1972; p.1243), Garrett and Grisham's *Biochemistry* (1999; p.244-247), The Merck Index (1992; Monograph 9255) and Drug Facts and Comparisons (1996; p.1064-1070).

Chopra teaches a dietary supplement or pharmaceutical dosage form for administration to patients comprising an effective amount of coenzyme Q and other additives, including phospholipids, tocopherols or tocopherol esters or other bioactive agents (see abstract, for example). Chopra teaches the use of phospholipids, such as phosphatidylcholine (known commonly as "lecithin", see Garrett and Grisham's *Biochemistry*, p.246), phosphatidyl ethanolamine, distearoylphosphatidyl choline, phosphatidyl serine, phosphatidyl glycerol, phosphatidic acid, phosphatidyl inositol or sphingomyelin (col.4, line 59-col.5, line 11), at an amount generally within the range from about 0.5% to about 25% or about 1% to about 20% by weight of the final composition (col.5, lines 27-31; see also claim 30). Chopra further discloses the use of bioactive agents, such as N-acetyl cysteine, alpha-lipoic acid (thioctic acid), acetyl-L-carnitine, resveratrol and other vitamins, such as A or C, or extracts of grape seed, pine bark, bilberry or milk thistle **or mixtures thereof** (emphasis added), at amounts within the range from about 0.01% to about 20% or about 0% to about 25% by weight of the composition (col.6, line 42-col.7, line 48; see also claims 27-28). The composition disclosed by Chopra may be formulated into cosmetic compositions, dietary supplements or pharmaceutical dosage forms, and may be administered orally via hard or soft gelatin capsules, as well as tablets, powders or

elixirs (col.8, lines 39-47), liquids, including mouth rinse (col.7, lines 49-50 and col.8, line 54), topically administered via creams or lotions, rectal or vaginal suppositories (col.8, lines 48-56), or via parenteral, intramuscular, intravenous, subcutaneous, transdermal or buccal administration (col.11, lines 55-61). Administration of the compositions taught by Chopra are generally administered from one to four times daily (col.9, lines 64-65) and may be used in the treatment of mitochondrial disorders or neurodegenerative diseases (col.10, lines 8-14). Chopra also teaches, "that dosage values will also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set fort herein are exemplary only and are not intended to limit the scope or practice of the claimed composition" (col.11, lines 38-47).

The differences between the Chopra reference and the presently claimed subject matter lie in that the reference does not teach:

(i) the use of (+/-) alpha-lipoic acid as recited in present claim 1;

(ii) the express proviso that alpha-lipoic acid and acetyl-L-carnitine are not administered together as recited in present claim 1, for example;

(iii) the use of an intranasal aerosol carrier as recited in present claim 5;

(iv) lipoic acid, acetyl-L-carnitine, N-acetyl cysteine or resveratrol as mitochondrial metabolites or promoters thereof as recited in present claim 7, for example;

(v) the particular dosage amounts as recited in the present claims or the use of synergistic effective amounts as recited in present claim 20; and

(vi) the use of the composition particularly for promoting cognitive function as recited in present claim 20.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) Although Chopra broadly discloses the use of alpha-lipoic acid, the reference is silent as to the particular use of (+/-) alpha-lipoic acid, understood by the Examiner to indicate either a combination of both the d- and the l-enantiomers or a racemic mixture of d- and l-enantiomers. However, such a mixture of enantiomers, the dl-form, was a pharmaceutically acceptable compound of the d- and l-enantiomers well known in the art at the time of the invention (see The Merck Index, Monograph 9255). It would have been well within the purview of a person skilled in the art at the time of the invention to employ the dl-form of alpha-lipoic acid in light of the broad teachings of Chopra, who discloses alpha-lipoic acid in general. Furthermore, such a person would be motivated to do so because such a mixture would be reasonably expected to function in the same or a similar manner to that of either enantiomer or a racemic mixture of both enantiomers.

(ii) Chopra does not expressly recite the proviso that the alpha-lipoic acid component of the composition and the acetyl-L-carnitine component of the composition are not administered together. However, the compositions disclosed by Chopra expressly recite the use of bioactive agents, including N-acetyl cysteine, alpha-lipoic acid (thioctic acid), acetyl-L-carnitine, resveratrol, **or mixtures thereof** (emphasis added; see col.6, line 42-col.7, line 48 and also

claims 27-28). Such a statement clearly provides for any combination of at least two of the bioactive agents listed above, including all possible combinations wherein alpha-lipoic acid and acetyl-L-carnitine are not administered in the same supplement. Thus, the Chopra reference is considered to meet the limitation of "with the proviso that the composition lipoic acid and the acetyl-L-carnitine are not administered together" (see present claim 1, for example).

(iii) Although Chopra does not expressly teach an intranasal aerosol formulation of the disclosed composition, it would have been obvious to a person of ordinary skill in the art to formulate the composition into any one of a number of other pharmaceutical formulations that were well known in the art at the time of the invention. Pharmaceutical formulations used for intranasal aerosol preparations, such as nasal sprays, were well known in the art at the time of the invention (see Drug Facts and Comparisons, 1996; p.1064-1070) and determination of the most appropriate formulation for administration would have been a matter well within the purview of the skilled artisan. Such a person would have been motivated to do so in order to enhance efficacy and tolerability of the pharmaceutical agents administered, especially in light of the teachings of Chopra, who states, "The most effective dosage form will depend upon the pharmacokinetics of the particular agent chosen as well as the severity of the condition in the patient to be treated" (col.9, lines 64-67).

(iv) The disclosure of Chopra does not expressly identify the alpha-lipoic acid, acetyl-L-carnitine, N-acetyl cysteine or lecithin components as "mitochondrial metabolites or promoters thereof". However, such a name is inconsequential to the fact that the compounds recited in the present claims are taught in the patent. The use of the label "mitochondrial metabolite or promoter thereof" does not render the presently claimed product patentably distinct from that of

the prior art because such a term does not impart any material or physical characteristic to the composition that is not otherwise present in the patented composition.

(v) Chopra teaches the use of phospholipids, such as phosphatidylcholine (known commonly as "lecithin", see Garrett and Grisham's *Biochemistry*, p.246), at an amount generally within the range from about 0.5% to about 25% or about 1% to about 20% by weight of the final composition (col.5, lines 27-31; see also claim 30). Chopra further discloses the use of bioactive agents, such as N-acetyl cysteine, alpha-lipoic acid (thioctic acid), acetyl-L-carnitine and resveratrol **or mixtures thereof** (emphasis added), at amounts within the range from about 0.01% to about 20% or about 0% to about 25% by weight of the composition (col.6, line 42-col.7, line 48; see also claims 27-28). Thus, 10 g of the composition would be comprised of about 1-2000 mg of an individual bioactive agent (for a dose range of about 0.01% to about 20% by weight) or about 0-2500 mg of an individual bioactive agent (for a dose range of about 0% to about 25% by weight) and about 50-2500 mg of an individual phospholipid (for a dose range of about 0.5% to about 25% by weight) or about 100-2000 mg of an individual phospholipids (for a dose range of about 1% to about 20% by weight. Therefore, the dose ranges taught by the Chopra reference clearly overlap with those of the presently claimed subject matter.

The Examiner acknowledges that the disclosure of Chopra does not expressly teach the particularly claimed dosage amounts of the present claims. However, the determination of the optimum dosage regimen, especially that used to promote cognitive or auditory function with the presently claimed active agents, would have been a matter well within the purview of one of ordinary skill in the art at the time of the invention. Such a determination would have been made in accordance with a variety of factors, such as the age, weight, sex, diet and medical condition

of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosage regimen that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific dosage amounts are not seen to be inconsistent with the dosages that would have been determined by the skilled artisan.

Furthermore, motivation to alter the dosage amounts of the components of the composition disclosed by the reference can be found also in Chopra, who expressly states, "that dosage values will also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set fort herein are exemplary only and are not intended to limit the scope or practice of the claimed composition" (col.11, lines 38-47).

The Examiner has noted the use of the phrase "synergistic effective amounts" in present claim 20. In the absence of a precise definition by Applicant, and in keeping with the guidance provided by the MPEP at §2111.01, the Examiner has interpreted the term "synergistic" to be defined by the meaning that is well known and accepted in the art. Stedman's Medical Dictionary has been relied upon for the art-accepted meaning of the term synergistic, which is equivalent to the term "synergetic", which means "working together" (see Stedman's Medical Dictionary, p.1243). Thus, the mere presence of an amount of at least two of the presently

claimed components together in the same composition administered for the same purpose clearly indicates that the amounts of the components administered would be "synergistic", in that they would be working together towards the same therapeutic purpose. Therefore, although Chopra does not expressly state the use of "synergistic" effective amounts of the components of the composition, the very nature of the concept of "synergistic", i.e., that the amounts must simply "work together", is taught by Chopra, who discloses the use of the presently claimed active components in a composition used for a common therapeutic purpose.

(vi) Applicant has stated in the present disclosure that the presently claimed composition "may offer benefits to patients with cognitive disorders such as non-specific dementias, Alzheimer's disease, and individuals suffering hearing loss" (see page 11, lines 3-5 of Applicant's acknowledgement). Applicant further states at page 12, lines 8-14, that "improvement in cognitive decline associated with neurodegenerative diseases" is seen with administration of the presently claimed composition. In light of the disclosure, the Examiner has understood the claim limitation recited in present claim 20 of "promoting cognitive function" to be the therapeutic objective of improving cognitive deficiencies associated with neurodegenerative diseases. Although Chopra expressly teaches the treatment of neurodegenerative diseases, but is silent as to the specific "promotion of cognitive function", a person of ordinary skill in the art at the time of the invention would have appreciated that the treatment of neurodegenerative diseases using the composition disclosed by Chopra in order to ameliorate the symptoms associated with the disease would necessarily promote the improvement of cognitive function in patients suffering from such a condition. The promotion of auditory function is not taught or suggested by the Chopra reference.

Conclusion

Rejection of claims 1-21 is deemed proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (8:30 AM-6:00 PM), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leslie A. Royds
Patent Examiner
Art Unit 1614

March 23, 2005

RAYMOND HENLEY III
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